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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/704,054	11/01/2000	Robert D'Amato	9516-0039-999	3798

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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/704,054	D'AMATO, ROBERT	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,29,73 and 76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,29,73 and 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/17/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 23, 29, 73, and 76 are pending

Applicants' response and amendments to the claims, filed 6/17/2009, are acknowledged and entered. Claims 27-28 and 74-75 have been cancelled by Applicant. Claims 23, 29, 73, and 76 are pending and under examination.

Response to Arguments

Any previous rejections and/or objections to claims 27-28 and 74-75 are withdrawn as being moot in light of Applicant's cancellation of the claims.

Applicants' arguments, filed 6/17/2009, have been fully and carefully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed 6/17/2009. The Examiner has considered the references cited therein to the extent that each is a proper citation. Please see the attached USPTO Form 1449.

Claim Rejections - 35 USC § 112 – 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 23 and 27-29 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (New Matter), is **withdrawn** in light of Applicant's amendments. While the Examiner disagrees with Applicant's arguments that

"blood-*born*" and "blood-*borne*" are synonymous, Applicant's amendment to the claims overcomes the rejection set forth in the previous Office Action.

The rejection of claims 23, 27-29, and 73-76 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (New Matter) regarding "therapeutically effective amount of thalidomide", is **withdrawn** in light of Applicant's amendments.

The rejection of claims 23 and 27-29 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is **withdrawn** in light of Applicant's arguments and amendments to the claims. Applicant's amendment, limiting the claims to "blood-born" tumors, is sufficient to over the rejection set forth in the previous Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23, 29, 73, and 76 remain rejected under 35 U.S.C. 103(a) as being unpatentable over **Vogelsang *et al.*** (N. Engl. J. Med., 1992, vol. 326, pages 1055-1058) (Reference C304 in IDS filed 11/7/2007) in view of **Kaplan** (USP No. 5,385,901).

Vogelsang *et al.* disclose administration of thalidomide to patients with chronic graft versus host disease whose **primary diagnosis** was chronic myelogenous leukemia (21 patients) (Table 1). The reference thus teaches administration to patients "having the blood-born tumors" as recited in claims 23 and 29 and to patients having "leukemia" as recited in claims 73 and 76.

Thalidomide was administered in an initial dose of 200 mg four times a day in adults (800 mg/day) and 3 mg per kg of body weight given four times a day in children (12 mg/kg/day) (page 1056, left column). These doses are "between approximately 0.5 and approximately 50

mg/kg/day of thalidomide" and "between approximately 1 and approximately 10 mg/kg/day" as recited in the instant claims. For example, 800 mg/day administered to an average human adult is approximately 10 mg/kg/day.

Thalidomide was found to be "safe and effective" for the treatment of chronic graft-versus-host-disease (Abstract).

Vogelsang *et al.* do not explicitly disclose in what form thalidomide was administered (*e.g.*, capsule, tablet, powder, solution, etc.).

However, Kaplan discloses compounds useful for controlling abnormal concentrations of TNF-α in patients (Abstract). The compounds of the invention include thalidomide (Figures and Examples; Claims). With regard to administration routes and forms, Kaplan *et al.* teach that the compounds of the invention can be administered orally in form of tablets, pills, lozenges, dragees and similar shaped and/or compressed preparations (col. 10, line 61 to col. 11, line 33).

Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to administer thalidomide to chronic myelogenous leukemia patients having graft-versus-host-disease *via* any administration known to be useful for such compounds. In this regard, Kaplan *et al.* teach and motivate one skilled in the art to administer compounds such as thalidomide *via* well known administration routes. As such, one skilled in the art would have been imbued with at least a reasonable expectation of success in formulating a dosage form of thalidomide for administration to chronic myelogenous leukemia patients having graft-versus-host-disease via the routes and in the dosage form instantly claimed with a reasonable expectation that such administration would be effective to treat graft-versus-host-disease in such patients as evidenced by Vogelsang *et al.*

Response to Arguments

Applicant traverses the instant rejection, stating that the pending claims recite a method of treating patients having blood-born tumors by administering thalidomide in a capsule. Applicant asserts that Vogelsang *et al.* does not teach or suggest any uses of thalidomide for treating patients with blood-born tumors or leukemia as recited in the instant claims. In response, the Examiner respectfully submits that Vogelsang *et al.* teach administration of thalidomide, in the doses instantly claimed, to patients whose **primary diagnosis** was chronic

myelogenous leukemia. Vogelsang *et al*. thus clearly and unequivocally teach administration to thalidomide to the same patients recited in the instant claims. The fact that Vogelsang *et al*. were evaluating thalidomide for treating graft-versus-host disease in these patients is not pertinent to the present rejection because the same compound is being administered in the same amounts and to the same patients as recited in the instant claims. As such, the effects of such treatment are a natural result of that treatment, whether directly observed by Vogelsang *et al*. or not.

Secondly, Applicant asserts that Vogelsang *et al*. teach away from the claimed invention by not disclosing the use of thalidomide for treating cancer but focusing only on treating graft-versus-host disease. In response, as discussed *supra*, the fact that Vogelsang *et al*. were evaluating thalidomide for treating graft-versus-host disease in these patients is not pertinent to the present rejection because the same compound is being administered in the same amounts and to the same patients as recited in the instant claims. As such, the effects of such treatment are a natural result of that treatment, whether directly observed by Vogelsang *et al*. or not. The instant claims do not preclude treating leukemia patients who also have graft-versus-host disease.

Thirdly, Applicant argues that the reference must be read in view of other art that teaches away from the claimed invention. However, as discussed above, the fact that Vogelsang *et al*. were evaluating thalidomide for treating graft-versus-host disease in these patients is not pertinent to the present rejection because the same compound is being administered in the same amounts and to the same patients as recited in the instant claims. As such, the effects of such treatment are a natural result of that treatment, whether directly observed by Vogelsang *et al*. or not. The instant claims do not preclude treating leukemia patients who also have graft-versus-host disease. The skilled artisan would expect thalidomide to be effective in treating graft-versus-host disease in these leukemia patients. The fact that Applicant has found that thalidomide will **also** treat the underlying leukemia, in addition to treating graft-versus-host disease, in these patients does not distinguish the claimed method from the cited prior art.

Fourthly, Applicant argues that Kaplan relates to the use of thalidomide for controlling abnormal concentrations of TNF-α and does not disclose that thalidomide is used for treating cancer, much less blood-born tumors or leukemia. However, the Examiner respectfully submits that Kaplan is relied on only for teaching that administration of thalidomide in tablets, pills, lozenges, dragees and similar shaped and/or compressed preparations (such as the claimed

capsules) was known in the art. As such, it would be obvious that thalidomide administered in Vogelsang was (or could reasonably and predictably be) administered in a capsule.

Fifthly, Applicant argues that the combined teachings do not provide the legally required reasonable expectation of success. When the references are combined, Applicant asserts that one skilled in the art is merely taught that thalidomide may be used to for treating graft-versus-host-disease, for example, but not cancers, much less blood-born tumors. The Examiner respectfully submits, however, that the cited prior art teaches that thalidomide is useful in treating patients with chronic graft versus host disease whose **primary diagnosis** was chronic myelogenous leukemia. These patients are clearly and unequivocally encompassed by the instant claims. The skilled artisan would expect thalidomide to be useful for such a purpose. The same compound is being administered in the same amounts and to the same patients as recited in the instant claims. As such, the effects of such treatment are a natural result of that treatment, whether directly observed by Vogelsang et al. or not. The instant claims do not preclude treating leukemia patients who also have graft-versus-host disease and Applicant has presented no factual evidence that leukemia was not treated in these patients.

Accordingly, the claims are deemed properly rejected for the reasons of record and as reiterated above. The skilled artisan would be motivated to administer thalidomide to patients chronic graft versus host disease whose **primary diagnosis** is chronic myelogenous leukemia and would be motivated with at least a reasonable expectation that such treatment would be effective.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
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